"CORRELATION OF SALIVARY GLUCOSE LEVEL WITH BLOOD GLUCOSE LEVEL IN DIABETES MELLITUS "

BY

REGISTER NUMBER: BG0121008

DISSERTATION

Submitted to KLE Academy of Higher Education and Research, Belagavi, Karnataka

In partial fulfilment of the requirements for the degree of

M.D. (Doctor of Medicine) in GENERAL MEDICINE

KLE Academy of Higher Education and Research
(Deemed-to-be University) Belagavi, Karnataka

Endorsement

This is to certify that the dissertation entitled
"CORRELATION OF SALIVARY GLUCOSE LEVEL WITH BLOOD GLUCOSE LEVEL IN DIABETES MELLITUS "is a bonafide research work done by **REG NO. BG0121008**.

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With reference to the above, we wish to inform you that your proposed research project titled **"CORRELATION OF SALIVARY GLUCOSE LEVEL WITH BLOOD GLUCOSE LEVEL IN DIABETES MELLITUS."** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

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ABSTRACT

Introduction: Saliva contains biomarkers such as different proteins, fatty acids, and carbhohydrates that, similar to blood, can reflect changes in human physiological activities, and so may serve as an alternative source for the early identification and monitoring of DM.

Objectives: To correlate salivary glucose level with blood glucose level in patients of diabetes mellitus patients at our tertiary care centre.

Methodology: The present Cross sectional Descriptive observational study was carried out at the Department of General Medicine, KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi involving 100 known cases of type 2 diabetes coming to Inpatient department . Study duration of 1 year from Aug 2023 to Aug 2024.

Results: Out of 100 cases, majority 47% were from above 60 years of age group ,followed by 32% from 51-60 years, followed by 13% from 41-50 years and 8% from 31-40 years. Mean age of the study population was 60.6±13.01 years.

We observed statistically significant positive correlation between fasting salivary sugar , fasting capillary sugar and fasting blood sugar levels, also between post prandial salivary sugar levels with post prandial capillary sugar and post prandial blood sugar levels in our study ($p<0.05$). **Conclusion:** Hence, we can conclude that saliva can be used as a non-invasive test for glucose estimation for screening patients of diabetes mellitus .

Key words: salivary glucose level, blood glucose level, diabetes mellitus

List of abbreviations

DM- Diabetes Mellitus

NDM- Non diabetes Mellitus

T2DM- Type II Diabetes Mellitus

OGTT-Oral Glucose Tolerance Test

IR-Insulin Resistance

PA-Physical Activity

ADA-American Diabetology Association

VLDL- Very low-density lipoprotein

HbA1c- Glycosylated Haemoglobin

CVD- Cardiovascular Disease

HNF-Hepatocyte Nuclear Factor

HL-Hepatic lipase

MODY-Maturity Onset Diabetes in Young

MRDM- Malnutrition Related Diabetes Mellitus

FBS -Fasting Blood Sugar

FCS- Fasting Capillary Sugar

FSS- Fasting Salivary Sugar

PPBS - Post Prandial Blood Sugar

PPCS- Post Prandial Capillary Sugar

PPSS- Post Prandial Salivary Sugar

Retinopathy

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Introduction

Diabetes Mellitus is a common metabolic disorder characterized mainly by high blood sugar levels, resulting from defective insulin secretion, insulin action, or both. It is a diverse group of diseases with various causes, including social, environmental, and genetic factors that act concurrently. Insulin is a hormone that regulates the body's metabolism of carbohydrates, proteins, and lipids at different levels. Long-term poor control of blood sugar levels can lead to disorders such as dyslipidemia, heart disease, central nervous system problems, and increased susceptibility to infections. [1-3]

"In India, Type 2 DM is a widespread disorder influenced by social and lifestyle changes. According to WHO, the global prevalence of diabetes was 170 million (2.8%) in 2002, and it's projected to reach 366 million (4.4%) or more by 2030." [4-6]

“Diabetes is more prevalent in developing countries, and India is on track to become the diabetic capital in the world, second to China in terms of prevalence. Currently, around 69.1 million people in India have diabetes, and this increased prevalence is attributed to the aging population and obesity. Type 2 diabetes, a chronic disease, is characterized by hyperglycemia and dyslipidemia due to underlying insulin resistance. As the disease progresses, it leads to microvascular and macrovascular complications”. [7]

The International Diabetes Federation (IDF) reported in 2019 that “approximately 4.2 million adults succumbed to diabetes and its complications, amounting to one death every 8 seconds.[8] By 2045, it is projected that a staggering 700 million adults worldwide will be managing some form of diabetes. [9] Presently, about half of the 463 million adults with diabetes are unaware of their condition, increasing their susceptibility to serious diabetes-related complications. Furthermore, recent studies

suggest that diabetes could go undiagnosed for up to seven years before clinical identification. During this period, individuals may develop potentially life-threatening issues such as retinal vascular disease, foot ulcers, renal failure, and various other forms of organ damage". [10-13]

Self-monitoring blood glucose, medical nutrition therapy, exercise therapy, patient education, and pharmaceutical therapy are the main clinical management techniques. Self-monitoring blood glucose is the cornerstone of all diabetes management techniques and is essential for managing the condition. [14, 15]

The non-invasive monitoring of diabetes mellitus (DM) through saliva has gained attention globally. [16,17] Saliva, an ultrafiltrate of blood, is seen as a source of clinical information reflecting the pathological state. Saliva has advantages as a diagnostic fluid due to its ease of collection and preservation, as well as its high-quality DNA. Therefore, it can be an excellent substitute for blood. [18-20]

Caixeta et al[21] stated, "salivary glucose was a potential outcome for screening, diagnosing, and monitoring DM, as they found a 95.2% accuracy of the laboratory test of salivary glucose in response to blood glucose." [22]

Rodrigues et al[23] stated, "saliva contains biomarkers such as different proteins, fatty acids, and carbs that, similarly to blood, can reflect changes in human physiological activities, and so may serve as an alternative source for the early identification and monitoring of DM."

Need for the study:

The non-invasive monitoring of diabetes mellitus (DM) through saliva has gained attention globally. Saliva, an ultrafiltrate of blood, is seen as a source of clinical information reflecting the pathological state. Saliva has advantages as a diagnostic fluid due to its ease of collection and preservation, as well as its high-quality DNA. Therefore, it can be an excellent substitute for blood.[23,24,25]

When people with diabetes have problems with the tiny blood vessels and base membrane of the salivary gland, the glucose in their saliva changes. This has made scientists consider using saliva to check for different illnesses.[26,27] It's important to keep a close eye on the amount of glucose in the blood of people with diabetes. Usually, a blood sample is taken with a needle or a finger prick for testing. These ways of collecting blood can be painful and stressful. It might be better to use saliva to check blood glucose levels and avoid the painful methods. [28,29,30]

Hence, we planned to conduct the study with the objective to correlate salivary glucose level with blood glucose level in diabetes mellitus patients at our tertiary care centre.

Objectives

To correlate salivary glucose level with blood glucose level in diabetes mellitus patients at our tertiary care centre.

Review of literature

This topic is reviewed under following heads:

1. Epidemiology of Diabetes Mellitus
2. Risk factors for DM
3. Role of salivary glucose in DM
4. Review of Studies conducted in the past on similar topic

1. Epidemiology of Diabetes Mellitus

Diabetes mellitus:

Diabetes is a significant global health issue, leading to serious health and socioeconomic impacts on individuals and populations. The increasing prevalence of diabetes is influenced by various demographic factors such as an aging population, socioeconomic changes, dietary and lifestyle patterns, migratory trends, and a rising incidence of obesity in both adults and children. [31]

Diabetes is a common metabolic disorder of the endocrine system, characterized by high glucose levels resulting from a combination of genetic and environmental factors. This can be due to decreased insulin secretion, insulin resistance, or both. [31]

Diabetes is a major health problem affecting a large population worldwide. According to the World Health Organization (WHO), the total number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. The prevalence of diabetes in adults aged 18 years and above has increased from 4.7% in 1980 to 8.5% in 2014. It increases with age, and approximately half of the cases occur in people older than 55 years. [32]

According to the International Diabetic Federation (IDF) 2015, India is one of the six main countries in the IDF South East Asia (SEA) region. Globally, 415 million people have diabetes, with 78 million people in the SEA region. By 2040, this number is projected to reach approximately 140 million in the SEA region. In India, there were 69.1 million cases of diabetes in 2015, with a prevalence of 8.7% in the adult population (20-79 years). Most diabetics live in underdeveloped and developing countries, accounting for up to 80% of cases. [32]

The prevalence of diabetes is increasing due to many factors such as dietary habits, sedentary lifestyle, ethnicity, obesity, hypertension, and genetic predisposition to the disease, all being major contributors to this epidemic. Uncontrolled diabetes is the major cause of micro and macrovascular complications such as blindness, kidney failure, heart attacks, stroke, and lower limb amputation. These long-term complications lead to increased mortality and morbidity among diabetic individuals. In 2012, according to WHO, 1.5 million deaths were directly related to diabetes. [32]

In absolute numbers, India will continue to be the country with the highest number of individuals living with diabetes, projected to have nearly 80 million people with diabetes by 2030. Diabetes is a common heterogeneous endocrine disorder, with a prevalence rising to approximately 20% in urban areas and 10% in rural populations. [32]

Figure 1: Worldwide prevalence of diabetes mellites[34]

Worldwide prevalence of diabetes mellitus. Global estimate is 382 million individuals with diabetes. Regional estimates of the number of individuals with diabetes (20–79 yearsof age) are shown (2013).

IDF Diabetes Atlas, the International Diabetes Federation, 2013.

Table 1: Prevalence of diabetes in India:[34]

Prevalence of diabetes and related risk factors			
	males	females	total
Diabetes	7.9%	7.5%	7.8%
Overweight	19.0%	23.9%	21.4%
Obesity	3.1%	6.5%	4.7%
Physical inactivity	9.2%	15.1%	12.1%

Classification of diabetes mellitus:

"Diabetes mellitus (DM) is categorized based on the development of high blood sugar levels. The American Diabetes Association (ADA) classifies DM into type 1 DM, Type 2 DM, and other specific types of diabetes, which include MODY, endocrinopathies, IGT & IFG, and GDM, among others".[34]

Type 2 DM:

Pathogenesis:

Ninety percent of instances of diabetes are type 2 diabetes. It's a complex, multifaceted illness with several underlying causes. It is typified by increased hepatic glucose production because of increased glycogenolysis and gluconeogenesis, as well as insulin resistance and increasing beta cell malfunction, which lead to altered insulin secretion and release. Patients with type 2 diabetes are known to have two main specific pathological deficiencies: beta cell dysfunction, or the pancreas's inability to produce enough insulin to compensate for insulin resistance, and decreased biological action of insulin on peripheral tissues, or insulin resistance.[34]

Patients with type 2 diabetes often have mild symptoms and are less likely to experience ketosis because their bodies do not depend on insulin to prevent the presence of ketones in the urine. This type of diabetes is frequently associated with obesity, and simple losing weight can often improve high blood sugar levels in these patients. While most people develop type 2 diabetes after the age of 40, it can also occur in younger individuals. The emergence of type 2 diabetes in children and adolescents is becoming a significant health concern.[34]

The pathological features of type 2 diabetes include increased absorption of intestinal glucose, reduced insulin secretion, and distinct changes in the beta cell mass, including insulin degradation and enhanced catecholamine. [34]

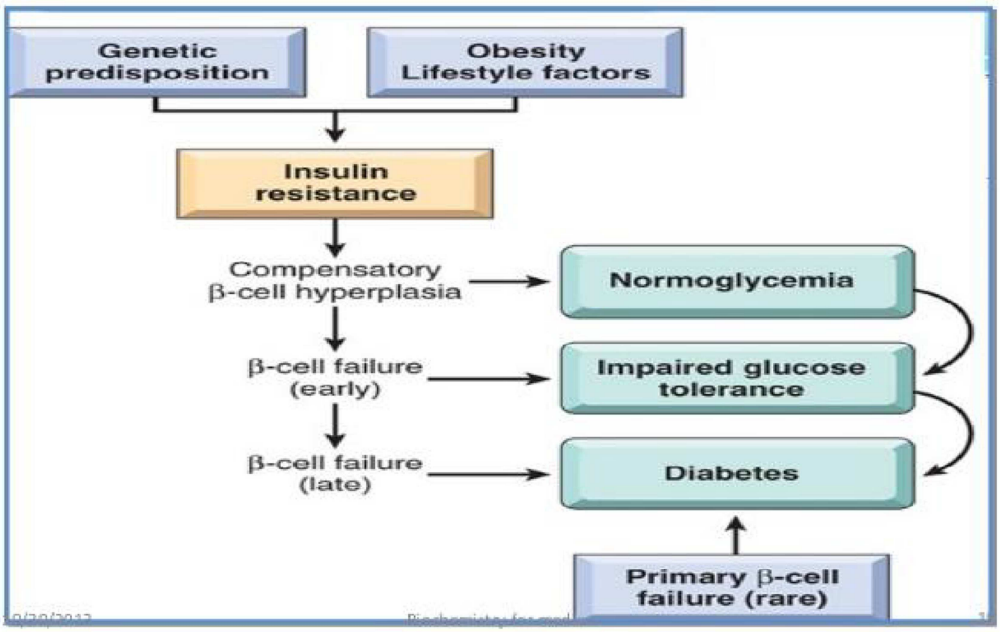

Figure 2: pathophysiology of type 2 DM[34]

2. Risk factors for DM:

Both modifiable and non-modifiable risk factors are associated with type 2 diabetes mellitus. Three of the most significant modifiable risk factors are obesity, weight gain, and physical inactivity.

Obesity:

When calorie intake and energy expenditure are out of balance, obesity results. A person's weight in kilograms divided by their height in meters squared yields their BMI. According to studies, there is a 12% rise in the risk of type 2 diabetes for every unit increase in BMI. Lean diabetes is another concept that has emerged in recent years.42 This type of diabetes develops in young guys from low socioeconomic backgrounds who were malnourished as children and whose

disease manifests early without ketosis. Beta cell failure is a common occurrence in these people. This entity has a multifactorial pathogenesis linked to a higher risk of cardiovascular death because of behavioral, environmental, and genetic variables. Speaking of the impact of obesity, namely central obesity, which is deposit An important risk factor for diabetes mellitus is adipose tissue in the abdomen and trunk. Waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-thigh ratio (WTR) are the surrogate metrics of central obesity. Newer methods such as DEXA, MRI, and CT can also be used to assess fat that is subcutaneous and intraabdominal. Insulin resistance can result from intra-abdominal fat alone, without considering the overall amount of body fat. [34]

● Physical Activity:

Movement of the body that results in an increase in energy expenditure caused by skeletal muscle contraction is referred to as physical activity. Conversely, exercise is a subset of physical activity (PA) that is carried out with the intention of improving physical fitness. Diabetes risk is inversely correlated with PA. By itself, PA lowers body weight and, hence, lowers the risk of obesity. Insulin sensitivity can also be improved by exercise. Research has indicated that while exercise quantity and duration are essential factors in lowering the incidence of diabetes, exercise length has a more significant role.[34]

● Sedentary Lifestyle:

Diabetes and obesity are both correlated with a sedentary lifestyle. When compared to people who did not get diabetes mellitus, those who develop diabetes exhibit higher levels of leisure sedentary behavior and television watching. This demonstrates a favorable correlation between a sedentary lifestyle and an increased risk of diabetes. Adiposity, inflammation linked to obesity, decreased lipoprotein lipase activity, triglyceride clearance, oral glucose load clearance, and

glucose-stimulated insulin secretion are all linked to sedentary behavior. The Diabetes Prevention Program (DPP), among other lifestyle therapies, is helpful in enhancing glucose metabolism. Reducing calories leads to weight loss, while physical activity (PA) helps keep the weight off. Watching TV for extended periods of time is linked to a sedentary lifestyle and increases the risk of diabetes. Watching television for two to ten hours a week increases the risk of diabetes by 66%. If you watch for more than 40 hours a week, the risk rises even further.

The likelihood of obesity has also increased by 23 percent. A 2-hour increase in sitting time at work is associated with a 5% higher chance of developing diabetes mellitus. The chance of developing diabetes at the outset can be lowered by 43% by leading an active lifestyle, which includes brisk walking for at least 30 to 45 minutes five times a week and watching less than 10 hours of television. Impaired glucose tolerance (IGT) is less likely to proceed to diabetes mellitus by 30–58% when moderate physical exercise is engaged in.[34]

Dietary variables: Diet is a complicated phenomenon consisting of many different foods and nutrients that interact in different ways. It varies depending on personal taste, cultural heritage, and socioeconomic considerations. Dietary measurements are made using food diaries and survey instruments. Dietary patterns, the absolute amount of nutrients consumed, the proportion of nutrients consumed relative to total calories, and the bioavailability of food components such as the glycemic index are used to evaluate diets.[34]

● Dietary fat: Obesity is linked to diets high in fat. The mechanisms involved include insulin-mediated signal transduction and its function, as well as changes in cell membrane composition brought on by dietary fat consumption, which affects membrane fluidity. High-fat, low-carb diets are positively correlated with type 2

diabetes (T2DM), yet the findings are inconsistent among research (32). It matters what kinds of fat and carbohydrates are consumed. Elevated consumption of polyunsaturated fatty acids and long-chain n-3 fatty acids (found in fish oil) is advantageous, but elevated consumption of saturated and trans fatty acids is detrimental.[34]

● Dietary carbs:

Compared to the intake of protein or fat, the consumption of carbohydrates directly challenges the beta cells. Therefore, a diet high in carbohydrates is linked to a higher risk of diabetes. This effect is influenced by the food's glycemic index and carbohydrate composition. [34]

● Glycemic index: This indicator calculates the amount of glucose that is released after eating. Foods having a high glycemic index cause glucose levels to fluctuate more. The pace at which glucose is absorbed determines the postprandial excursions. It also relies on the amount of fiber consumed and the kind of carbohydrate—complex or simple. It's unclear if eating foods low in glycemic index will lower your risk of developing diabetes.[34]

● Other Food Intake: Consuming a lot of fiber lowers the chance of developing diabetes. However, the mechanism is not understood. It can be explained by a high-fiber diet with a low glycemic index. A high vegetable diet lowers the chance of developing diabetes. Diabetes risk is lowered by antioxidants in fruits, such as carotenoids and tocopherols, which are linked to high fiber and vitamin intake. A low-fat, high-fiber Pima diet has been shown to lower the incidence of diabetes mellitus (DM). [34]

● Inflammation:

It has been discovered that inflammation serves as the fundamental causal component that causes atherosclerosis to develop. C- reactive protein, a sign of subclinical inflammation, is linked to metabolic disorders such as insulin resistance, obesity, hypertriglyceridemia, low HDL cholesterol, and low HDL cholesterol. Elevations in CRP are linked to a higher chance of developing diabetes. Subclinical inflammation has therefore emerged as a key factor in type 2 diabetes (T2DM), and research has demonstrated that using anti-inflammatory medications, such as high-dose aspirin, lowers insulin resistance and enhances glucose tolerance. [34]

● Smoking: Smoking poses a separate risk for the onset of diabetes. According to studies, smoking raises the risk of DM by 45%.[47] Additionally, current smokers had the highest mean HbA1c concentrations, while non-smokers have lower values. Additionally, there is a dose-response correlation between HbA1c levels and pack-years smoked, which is a measure of daily cigarette consumption. Insulin resistance is also linked to smoking. Smokers' levels of HDL cholesterol are lower and their plasma triglycerides are higher. Smoking-related oxidative stress leads to endothelial dysfunction, which makes the liver and muscles insulin resistant. [34]

3. Role of salivary glucose in DM

Saliva

Flow Rate of Saliva

Salivary flow rates are highly variable and stabilize after the age of 15 years; therefore, they should be interpreted in a clinical context. The numbers depicted in this section are averages projected from studies on the general population. The range of normal unstimulated salivary flow is 0.1 mL/min and above; in the stimulated state, it is 0.2 mL/min and above. On average the unstimulated flow rate is 0.3 mL/min, and the stimulated flow rate is 7 mL/min at maximum. Stimulated saliva is thought to contribute as much as 80% to 90% of the average daily salivary production. This leads to an average daily saliva secretion of around 1000 to 1500 mL or an average flow of 1 mL/min. [29,30] Salivary flow in the unstimulated state is produced primarily by the submandibular glands (71%); the parotid and sublingual glands produce 25% and 3% to 4% of the flow, respectively. The minor salivary glands account for trace amounts of saliva. Once stimulated, the relative contributions of the parotid and submandibular glands are reversed, and the parotid gland supplies two-thirds of the salivary flow.

Studies that have specifically addressed hypofunction of the salivary gland have defined the critical range that separates a person with normal gland function from someone with salivary gland hypofunction as unstimulated whole salivary flow rates between 0.12 and 0.16 mL/min.

The diagnosis of salivary hypofunction is often difficult to make, given the wide range of salivary flow rates that are accepted as normal. A more reliable means of diagnosing hypofunction is possible if an individual base record of saliva flow has

been established. Salivary gland hypofunction can then be defined as a 50% reduction in the individual base saliva flow rate. About 30% of the population reports some degree of dry mouth. In general, oral-related effects of salivary hypofunction are reduced preparation of food for digestion and taste and an increased susceptibility of oral structures to disease. Although decreased concentrations of salivary mucins and decreased resting salivary flow rates have been associated with increasing age, in general, no substantial age-related changes in the secretory responsiveness of salivary cells are apparent. Furthermore, factors endemic to the geriatric population—such as polypharmacy, poor nutritional status, and systemic diseases—also contribute to salivary gland hypofunction. At present, the exact role of advancing age on the average daily production of saliva and xerostomia is unknown.

Salivary secretion is controlled by a salivary center in the medulla, which is triggered by specific stimuli that include the mechanical act of chewing and gustatory and olfactory stimuli. The stimulation of salivary flow with mastication is thought to be a reflexive response mediated by receptors in the oral mucosa, muscles of mastication, and temporomandibular joint. These receptors stimulate the salivary nucleus, which in turn increases the parasympathetic stimulation to the salivary glands, resulting in increased salivary flow.

Interestingly, the increase in salivary flow is thought to be directly proportional to the applied chewing force. Gustatory stimuli are the most potent stimuli to the salivary center and elicit as much as a 10-fold increase in salivary flow. Acidic tastes lead to the greatest increases in saliva flow, whereas sweet tastes are the least stimulating. Olfaction is the weakest of the salivary center triggers. Furthermore, habituation is thought to occur with repeated presentation of the same food cues, which leads to a

decrease in stimulation of the saliva center and saliva flow. Dishabituation occurs with the presentation of novel food cues.

Many other factors can also influence salivary flow. These factors include

(1) circadian rhythm;

(2) psychic factors such as pain, depression, and anticipation of food;

(3) medications;

(4) local or systemic diseases; and

(5) hormones.

Isolating and studying the effect of a specific factor is often difficult because many of these stimuli work in concert to affect salivary flow. Diurnal variation in salivary flow has been reported, with maximal flow rates in the late afternoon and minimal flow rates at night. Decreased salivary output at night may be secondary to a decrease in ambient light and/or arousal state, both of which affect salivary gland function.

Medications with anticholinergic properties decrease salivary flow; this includes most antidepressants. Dehydration can influence salivary gland output: with losses of 8% of body water; the result is cessation of salivary flow. Decreased salivary output is also noted during the “fight or flight” response, which results from an increased sympathetic response and/or central inhibition of parasympathetic output. The sympathetic nervous system has also been proposed to play a role in the reduction of saliva flow after exercise via the constriction of blood vessels that supply the salivary glands.

Salivary flow is uneven throughout the mouth secondary to the location of the ducts that empty the parotid and salivary glands. Intraoral flow volume is the highest in the mandibular lingual area and the lowest in the area of the maxillary incisors and interproximals. These areas of higher- and lower-volume flow regions have been referred to as “salivary highways and byways.” The regional clearance rate of acid produced from bacteria is directly influenced by regional variations in flow within the mouth.

Therefore, unless mechanical methods of cleaning are employed, acid byproducts may stay in extended contact with oral tissues in salivary byways. Furthermore, it is hypothesized that saliva offers various forms of protection at various intraoral regions due to the variable volumes of saliva and salivary ingredients originating from different glands.[35]

Composition of Saliva

Saliva's numerous functional qualities are made possible by a wide range of organic and inorganic chemical components. The majority of the inorganic component is made up of nitrogenous products like urea and ammonia as well as electrolytes including sodium, potassium, calcium, magnesium, bicarbonates, and phosphates. The organic component consists of various protein groups, including mucins, enzymes, and immunoglobulins. The composition of entire saliva at any given time might vary greatly since the final saliva product is an aggregate of the saliva produced by numerous glands, each with varied secretory characteristics. This diversity is further increased by the fact that each gland's secretory properties vary depending on the kind of stimulation that causes saliva to be produced.

Furthermore, variations in the quantity of inorganic substances released or reabsorbed in the salivary ducts will cause variations in the electrolyte composition of saliva based on flow rates. Overall, entire saliva has a pH range of 5.75 to 7.05, a specific gravity of 1.002 to 1.0012, and a composition of about 99.5% water. Saliva's osmolarity is primarily dictated by four main ions, namely sodium, potassium, chloride, and bicarbonate. Although phosphate has a limited function in salivary buffering, bicarbonate is the primary salivary buffer system, and as such, the pH of saliva is mostly determined by its CO2 level. Because electrolytes enter saliva through an active process, the composition of electrolytes in saliva is largely unaffected by plasma concentrations. Because organic chemicals passively diffuse into saliva, salivary concentrations of these substances mirror those of plasma. [35]

Table 2: Flow Rates and Composition of Saliva in Normal Adults[35]

	Parotid Gland	Submandibular Gland
Stimulated flow rate (mL/min/gland)	0.7	0.6
INORGANIC CONSTITUENTS (mEq/L)		
K^+	20	17
Na^+	23	21
Cl^-	23	20
HCO_3	20	18
Ca^{2+}	2	3.6
Mg^{2+}	0.2	0.3
HPO_4^{-2}	6	4.5
ORGANIC CONSTITUENTS (mg/dL)		
Urea	15	7
Ammonia	0.3	0.2
Uric acid	3	2
Glucose	<1	<1
Cholesterol	<1	—
Fatty acids	1	—
Total lipids	2–6	2–6
Amino acids	1.5	—
Protein	250	150

Modified from Mandel ID: Sialochemistry in diseases and clinical situations affecting salivary glands. *Crit Rev Clin Lab Sci* 12(4):321–366, 1980.

Inorganic Component

Sodium (Na^+) and potassium (K^+) are the major cations present in saliva.

The salivary concentration of these ions depends on the type of gland from which they are secreted as well as the type and amount of stimulation to the gland. In general, the concentration of these electrolytes in the parotid gland is higher than in the submandibular gland. When the salivary flow rate is low, the ratio of Na^+ to K^+ is also low. This ratio increases as the flow rate increases because of decreased reabsorption of Na^+ at higher flow rates. As with Na^+ and K^+, the salivary concentration of Ca^{2+} also varies with the type of gland from which it is secreted and with salivary flow rates. Salivary calcium concentrations, however, appear to be flow dependent only at high flow rates. In addition, unlike salivary Na^+ and K^+, the concentration of Ca^{2+} in saliva from the submandibular gland (3.4 to 4.4 mEq/L) is almost twice that of the parotid gland (1.4 to 2 mEq/L). Calcium is distributed in saliva as a free ion, or it may be bound to protein or found in complexes with carbonate, phosphate, or lactate. Salivary magnesium concentrations from the parotid and salivary glands are fairly equivalent and represent roughly two-thirds of the plasma concentration. [35]

Phosphate, bicarbonate, and chloride are the main cations found in saliva. The salivary gland and parotid gland both have comparable salivary chloride concentrations, which are lower than those of plasma. The concentrations of salivary chloride are dependent on flow and drops as flow rates drop. Salivary bicarbonate concentrations can be as low as 5 mEq/L when at rest, and they can rise to levels higher than plasma (27 mEq/L) in response to stimulation. Salivary bicarbonate is produced by the gland's metabolism and plasma. One of the minor buffers, salivary phosphate is present at values noticeably greater than those of serum. Phospholipids

and tiny levels of pyrophosphate contain the majority, of which approximately 10% of salivary phosphate that is found in the ester form.

Fluoride and iodine are two minor inorganic components found in saliva. Saliva has an iodine content of around 10 to 15 µg/mL. Salivary fluoride content is somewhat higher in people who use fluoridated toothpaste or drink fluoridated water, although it is about comparable to that of plasma. Fluoride from sparingly soluble deposits on the teeth and soft tissues is released into saliva over an extended period of time in these people. It is thought that these slight increases in salivary fluoride levels are crucial in halting the development of dental caries.

Organic Components

Proteins or protein-containing moieties comprise the majority of the organic components of saliva. The concentration of protein is higher in stimulated parotid than in stimulated submandibular secretions [29,30]. On average, the protein content of whole saliva is 200 mg/100 mL, which is about 3% of the protein concentration in plasma. [31] Careful analysis of whole saliva, as well as saliva from each of the major salivary glands, has revealed the presence of distinct families of proteins within saliva, and each family contains multiple members. The structural variations of individual family members arise by a combination of genetic and posttranslational events. The major salivary components of saliva range in size from small histatins (2 to 4 kDa) to larger mucins (>1000 kDa;). [35]

4. **Studies conducted in the past on similar topic:**

Cui Y et al[36] in 2022 conducted the study and stated that, " the objective to identify an ideal saliva collection method and to use this method to determine the population and individual correlations between salivary glucose and blood glucose levels in DM patients and healthy controls. Finally, an analysis of the stability of the individual correlations is conducted. This study included 40 age-matched DM patients and 40 healthy controls. In the fasting state, saliva was collected using six saliva collection methods, venous blood was collected simultaneously from each study participant, and both samples were analyzed at the same time using glucose oxidase peroxidase. A total of 20 DM patients and 20 healthy controls were arbitrarily selected from the above participants for one week of daily testing. The correlations between salivary glucose and blood glucose before and after breakfast were analyzed. Finally, 10 DM patients and 10 healthy controls were arbitrarily selected for one month of daily testing to analyze the stability of individual correlations. Salivary glucose levels were higher in DM patients than healthy controls for the six saliva collection methods. Compared with unstimulated saliva, stimulated saliva had decreased glucose level and increased salivary flow. In addition, unstimulated parotid salivary glucose was most correlated with blood glucose level (R2 = 0.9153), and the ROC curve area was 0.9316, which could accurately distinguish DM patients. Finally, it was found that the correlations between salivary glucose and blood glucose in different DM patients were quite different. The average correlation before breakfast was 0.83, and the average correlation after breakfast was 0.77. The coefficient of variation of the correlation coefficient before breakfast within 1 month was less than 5%. Hence they concluded that unstimulated parotid salivary glucose level is the highest and is most correlated with blood glucose level, which can be accurately used to distinguish DM

patients. Meanwhile, the correlation between salivary glucose and blood glucose was found to be relatively high and stable before breakfast. In general, the unstimulated parotid salivary glucose before breakfast presents an ideal saliva collecting method with which to replace blood-glucose use to detect DM, which provides a reference for the prediction of DM."[36]

Dharmakeerthi et al[37] in 2021 reported that, "correlation between blood glucose level and salivary glucose level of type 2 diabetic mellitus patients. A cross sectional study was conducted at a diabetic clinic in a teaching hospital in Sri Lanka. Blood samples were collected to analyze fasting blood glucose and HbA1c levels. Unstimulated whole saliva samples were collected to measure salivary glucose level and salivary flow rate. Pearson's correlation was applied to determine the association between salivary glucose, blood glucose and HbA1c levels. A total of 120 type 2 diabetes mellitus patients and 31 healthy controls were participated. Salivary glucose level was significantly higher in DM patients than healthy individuals. Fasting blood glucose level was significantly correlated with salivary glucose levels among DM patients ($r = 0.201$, $p = 0.027$). A significant relationship was also observed between HbA1c and salivary glucose levels among DM patients ($r = 0.288$, $p = 0.031$). So, they concluded that measuring salivary glucose levels may have potential to be used as an alternative non-invasive procedure to screen, diagnose and monitor the glycemic conditions of the DM patients".[37]

Mishra N. et al[38] in 2019 stated that, "the objective to correlate salivary glucose, blood glucose levels and oral colony forming units of Candida albicans and to evaluate whether saliva can be used as noninvasive means to measure glycemic status in type II diabetics without the need for the invasive procedure. The study included 100 type II diabetic patients (group I) of both genders with age 40 years and above

and100 healthy patients (group II), age and sex matched with the study group. Group I include uncontrolled and controlled diabetics as groups IA and IB, respectively. Salivary glucose measurement was done using the enzymatic colorimetric method and blood glucose levels measured by doing venepuncture and centrifuged. The oral candidal carriage was calculated by incubation in Sabouraud's dextrose agar supplemented with chloramphenicol and incubated aerobically for 48 hours. To compare the mean values Z test was applied. To determine the relationship between two variables Pearson's correlation coefficient was used. The salivary glucose levels showed a significant correlation with blood glucose levels. The salivary candida carriage was higher in uncontrolled as compared to controlled diabetics and healthy individuals. They concluded that positive correlation was obtained between salivary glucose and blood glucose in diabetics and candidal carriage has a positive correlation with blood glucose levels. This salivary glucose and blood glucose levels correlation confirms its use to find glycemic status in diabetic patients."[38]

Golamari UMR et al[39] in 2019 stated, "cross-sectional study of a group of 100 diabetic patients and 100 healthy controls, conducted in the Department of General Medicine, SRM medical college hospital. The mean difference in the salivary glucose between diabetic and non-diabetic population was compared using unpaired t-test. There was a strong positive association between FBS (fasting blood sugar) and salivary glucose in the overall population. There was a strong positive correlation between FBS and Salivary glucose in FBS <200. There was a moderate positive association between FBS and salivary glucose in people with FBS value between 200 to 300 mg/dl. There was a weak positive association between FBS and salivary glucose in people with FBS value >300 mg/dl, which was statistically not significant. There was a strong positive correlation between HbA1c and salivary glucose in the

overall population. So the author concluded that there appears to be a strong positive association between fasting blood sugar and salivary glucose value in both study groups. But the correlation seems to be relatively weak in fasting blood sugar range above 300 mg/dl." [39]

Afreen Nadaf et al[40] in 2017 in their study stated that, "the objective to assess the correlation of fasting blood glucose level (FBG) and fasting salivary glucose level (FSG) in diabetic and non-diabetic patients. An experimental study was conducted in 60 patients who fulfilled the selection criteria. Patients were categorized into 2 groups -30 patients with diabetes mellitus (Group A) and 30 healthy non-diabetic patients (Group B). The fasting blood and unstimulated saliva samples were collected from the patients. These samples were then subjected for analysis of glucose in blood and saliva using HEXOKINASE reagent in Abbot C4000 Automatic analyzer and the results were recorded. A statistically significant difference (p=0.0001*) was found between the fasting blood glucose level between the 2 groups with mean FBG level in group A (182.23±12.67) and fasting blood glucose level among group B was 73.59±7.56. The mean FSG was higher in diabetic group (13.13± 3.2) than in non-diabetic group (0.72±0.08). A highly statistically significant correlation was found between fasting salivary glucose and fasting blood glucose in both the groups. The present study clearly depicts that fasting salivary glucose is increased in diabetics and this finding was statistically significant. On the basis of the findings, it was concluded that salivary glucose levels could serve as a potentially non-invasive adjunct to monitor glycemic control in diabetic patients." [40]

Kumar K. et al[41] in 2017 conducted, "Higher percentage of diabetic patients had good knowledge and perception about diabetes and blood glucose maintenance than healthy subjects. Among diabetics mean salivary glucose level was 9.98±3.01 mg/dl.

This was much higher as compared to non-diabetic individuals (7.56±1.37 mg/dl). Mean salivary glucose levels were found to be significantly correlated with mean blood glucose levels of diabetics (r= 0.811) and non-diabetics (r= 0.506). This study suggested that saliva may become an alternative to blood for lab diagnostic procedures if further extensive studies are done in future." [41]

Gupta S. et al[42] in 2017 quoted, "in cross-sectional study with 120 patients, who were categorized as 40 controlled diabetics, 40 uncontrolled diabetics and 40 healthy, age-.and sex-matched individuals constituted the controls. The blood and unstimulated saliva samples were collected from the patients at the different intervals for fasting, random and postprandial levels. The mean SGLs were higher in uncontrolled and controlled diabetic groups than in nondiabetic group. A highly statistically significant correlation was found between fasting saliva glucose and fasting blood glucose in all the groups. With increase in BGL, increase in SGL was observed in patients with diabetes suggesting that SGL can be used for monitoring glycemic level in DM." [42]

Akasapu A. et al[43] in 2017 reported, "involving total of 200 subjects (100 subjects in each group). Based on their clinical history, two groups were created; group I (Diabetic patients) & group II (Healthy controls). Both the groups were screened for plasma and salivary glucose levels. The mean values of blood glucose were 115.230mg/dl ±21.4 for control group and 213.546mg/dl±68 for diabetic group. The mean values of salivary glucose were 4.272mg/dl±2.23 for healthy controls and 13.603mg/dl±5.599 for diabetic group. The correlation coefficient between serum glucose and salivary glucose was calculated and the 'r' value was found to be 0.7686, which was highly significant (P value 0.01). It is important to note that the study group's significance was significantly higher than the control group's. These results

imply that measuring blood glucose levels using saliva may be a useful diagnostic technique. Nevertheless, in order to validate our findings, more research with a wider range of sample sizes is required." [43]

Gupta S. et al[44] in 2015 reported, "serum and salivary glucose levels of 200 subjects (100 diabetic subjects and 100 nondiabetic subjects) were estimated by glucose oxidase method. Glycosylated hemoglobin levels were also measured in randomly selected 40 diabetic subjects. The findings of present study revealed a significant correlation between salivary and serum glucose levels in both diabetic and nondiabetic subjects. No significant relationship was observed between salivary glucose levels and gender or age in both diabetics and nondiabetics and between salivary glucose levels and duration of diabetes in diabetics. On the basis of the findings, it was concluded that salivary glucose levels could serve as a potentially non-invasive adjunct to monitor glycemic control in diabetic patients." [44]

Kumar S. et al[45] in 2014 conducted the study, "with the objective to the correlation between blood glucose levels and salivary glucose levels in type 2 diabetic patients, to study the relationship between salivary glucose levels and oral candidal carriage in type 2 diabetic patients and to determine whether salivary glucose levels could be used as a non-invasive tool for the measurement of glycemic control in type 2 diabetics. The study population consisted of three groups: Group 1 consisted of 30 controlled diabetics and Group 2 consisted of 30 uncontrolled diabetics based on their random nonfasting plasma glucose levels. Group 3 consisted of 30 healthy controls. Two milliliters of peripheral blood was collected for the estimation of random nonfasting plasma glucose levels and glycosylated hemoglobin (HbA1c). Unstimulated saliva was collected for the estimation of salivary glucose. Saliva was collected by the oral rinse technique for the estimation of candidal counts. The

salivary glucose levels were significantly higher in controlled and uncontrolled diabetics when compared with controls. The salivary candidal carriage was also significantly higher in uncontrolled diabetics when compared with controlled diabetics and nondiabetic controls. The salivary glucose levels showed a significant correlation with blood glucose levels, suggesting that salivary glucose levels can be used as a monitoring tool for predicting glycemic control in diabetic patients. The present study found that estimation of salivary glucose levels can be used as a non-invasive, painless technique for the measurement of diabetic status of a patient in a dental set up. Increased salivary glucose levels leads to increased oral candidal carriage; therefore, oral diagnosticians are advised to screen the diabetic patients for any oral fungal infections and further management." [45]

Materials and Methods

Study setting: Department of General Medicine, KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Study population: Known cases of diabetes coming to IPD

Study period: One year

Study design: Cross sectional Descriptive observational study

Sample size:

Formula for sample size calculation:

(**Source for formula:** Source: Patrikar S. In Text book of Community Medicine. 1st Ed, 2009. Ed. Bhalwar R. Dept of Community Medicine. AFMC Pune. Publ. WHO India Office, New Delhi) [46]

$$n = \{(\frac{z1+Z2}{Cr})^2 + 3\} \qquad Cr = \frac{1}{2}\{LOGe\frac{(1+r)}{(1-r)}\}$$

Ref of article: Golamari UMR, Natarajan MSS, Lakshmanan A, Balakrishnan RK. Correlation between salivary glucose and blood glucose levels in diabetic and non-diabetic individuals. Int J Adv Med 2019;6:1220-5.[39]

Variable considered for calculation of sample size:

Correlation between fasting salivary glucose and fasting blood glucose is considered here for sample size calculation

N	Guestimate of Correlation coefficient	0.513
Cr	Fisher's arctanh transformation	0.566
1-α	Set level of confidence (<1.0)	0.99
1-β	Set level of power of test (<1.0)	0.9
Z1	Z value associated with alpha	2.575
Z2	Z value associated with beta	1.281
n	**Minimum Sample size**	**50**

Minimum sample size for our study would be 50, but we planned to include total 100 cases of diabetes in our study fulfilling the eligibility criteria

Sampling technique: Simple Random sampling method

Inclusion criteria:

- Confirmed type 2 diabetic patients (age above 30 years) of both gender
- Consenting to take part in the study

Exclusion criteria:

- People who had surgery on their salivary glands in the past or who have received radiation therapy to the head and neck area.
- Those not willing to participate
- Pregnant women

Variables used in study: Age, Gender, fasting salivary glucose level, Fasting blood sugar level,fasting capillary sugar level , post prandial blood sugar , post prandial capillary sugar level and postprandial salivary glucose,Hba1c.

Methods of data collection:

Every participant received comprehensive information about the research and provided their signed consent. The Helsinki guidelines were adhered to. A structured questionnaire was utilized to gather information about blood glucose management, diabetes mellitus, and educationalstatus.

Gathering of specimens: After fasting through the night, samples were gathered in the morning. Patients with diabetes were instructed to take their prescribed medication.

Saliva: - Over the course of five minutes, about two milliliters of unstimulated whole saliva were spit into a sterile container. Before saliva was collected, the subjects were instructed to rinse their mouths with clean water. The saliva sample that was obtained was either examined right away or kept in the refrigerator for no longer than two hours. After that, it was centrifuged for ten minutes at 3000 RPM. Salivary glucose was measured in the obtained supernatant solution.

1) Post prandial saliva is collected into a saliva collector after 2 hrs of meal, after rinsing the mouth clean water.

2) Serum: - Aseptic circumstances were upheld. A forearm median cubital vein was used to draw 2 ml of intravenous blood, which was then centrifuged for 10 minutes at 3000 RPM. The amount of sugar in the obtained serum was next examined.

3) Venous blood and saliva samples were taken, concurrently the measurement of capillary blood glucose was done using a glucometer.

4) Serum and Salivary Glucose Determination: - The Glucose Oxidase Peroxidase (GOD-POD) method was used to measure serum and salivary glucose. The assaying process was carried out using a semi-autoanalyzer.

Subjects' samples were taken in the morning, from 7:00 to 11:00 a.m. The unstimulated whole saliva was used in this investigation to measure the salivary glucose level. Two hours before to saliva collection, all participants were asked not to eat, brush their teeth, or smoke.

The saliva collector was to be filled with the subjects' spitted saliva. To reduce microbial contamination, saliva collected within the first 30 seconds was eliminated at the beginning. In order to estimate the salivary glucose levels, the patients were advised to rinse their mouths with tap water, spit two or three times, and then spit the saliva that collected in their mouths into the sterile sample collection container for the next ten minutes.

HbA1c and fasting blood sugar (FBS) readings were taken.

The values were recorded, and reports were documented.

Saliva samples were taken, and the levels of fasting salivary sugar (FSS) were determined. During the sample collection, every patient was sitting up straight and tilting their head forward. The clear supernatant from each unstimulated salivary sample was used to estimate the amount of glucose after it was centrifuged for ten minutes at 3000 rpm.

Statistical analysis:

Data was gathered utilizing a proforma for structure. Data entered into an MS Excel spreadsheet was analyzed with IBM USA's SPSS 24.0 edition. Poisson data was used to express qualitative data. Standard deviation and mean were used to express

quantitative data. Using Fischer's exact test and Chi square, an association between two qualitative variables was observed. To determine whether or not the mean difference between the groups is significant, the unpaired t test was used to compare the mean and SD between the two groups. Each variable's descriptive statistics were provided using the terms mean, standard deviation, and standard error of mean. The Pearson's correlation coefficient test was used to determine the correlation between two qualitative variables.

A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

Results

Table 1: Distribution according to age group

		Frequency	Percent
Age group in years	31-40	8	8.0
	41-50	13	13.0
	51-60	32	32.0
	>60	47	47.0
	Total	100	100.0

We included confirmed cases of type II diabetes in our study. Out of 100 cases, majority were from above 60 years age group i.e. 47% followed by 32% from 51-60 years age group followed by 13% from 41-50 years and 8% from 31-40 years. Mean age of the study population was 60.6±13.01 years.

Figure 1: Bar diagram showing Distribution according to age group

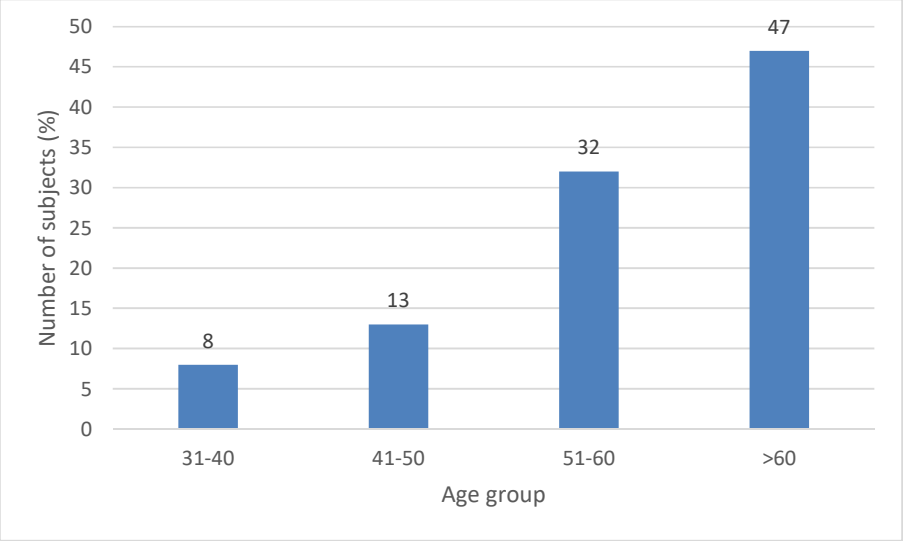

Table 2: Distribution according to gender

		Frequency	Percent
Gender	Male	62	62.0
	Female	38	38.0
	Total	100	100.0

62% of the cases were males and 38% were females.

Figure 2: Pie diagram showing Distribution according to gender

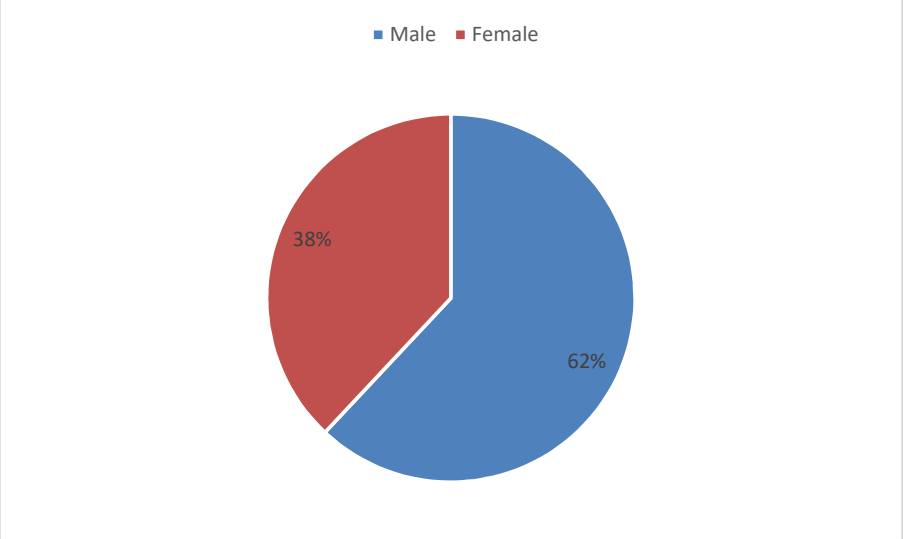

Table 3: Correlation of fasting capillary sugar with fasting salivary sugar

		FSS
FCS	Pearson Correlation	.298**
	p value	0.003
	Inference	Positive correlation

We observed statistically significant positive correlation of fasting capillary sugar with fasting salivary sugar($p<0.05$).

Figure 3: Scatter diagram showing Correlation of fasting capillary sugar with fasting salivary sugar

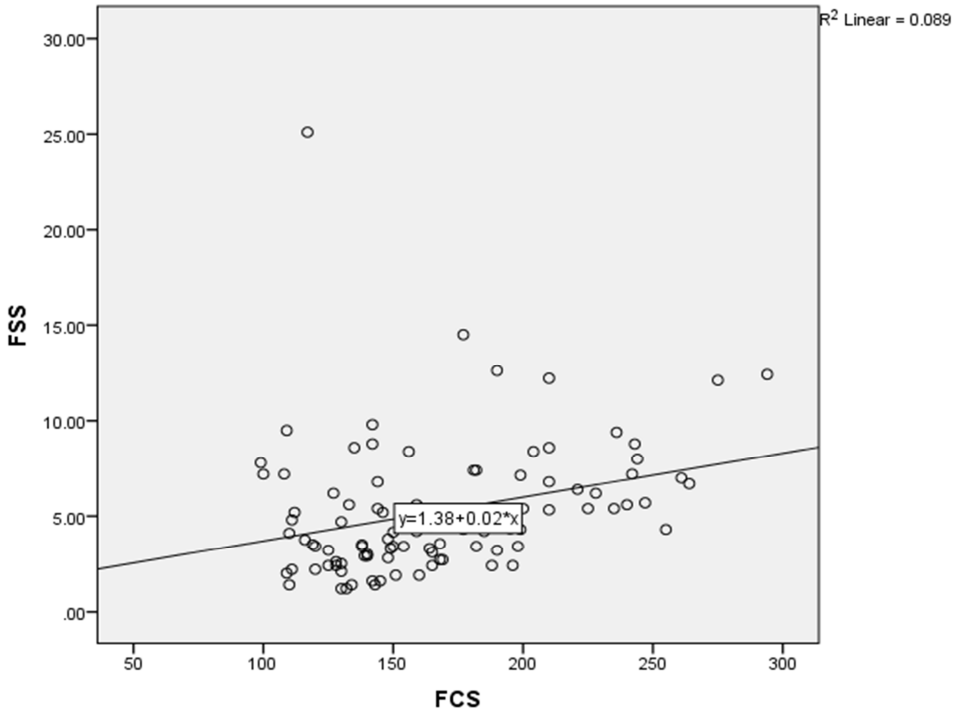

Table 4: Correlation of fasting blood sugar with fasting salivary sugar

		FSS
FBS	Pearson Correlation	0.317
	p value	0.001
	Inference	Positive correlation

We observed statistically significant positive correlation of fasting blood sugar with fasting salivary sugar ($p<0.05$).

Figure 4: Scatter diagram showing Correlation of fasting blood sugar with fasting salivary sugar

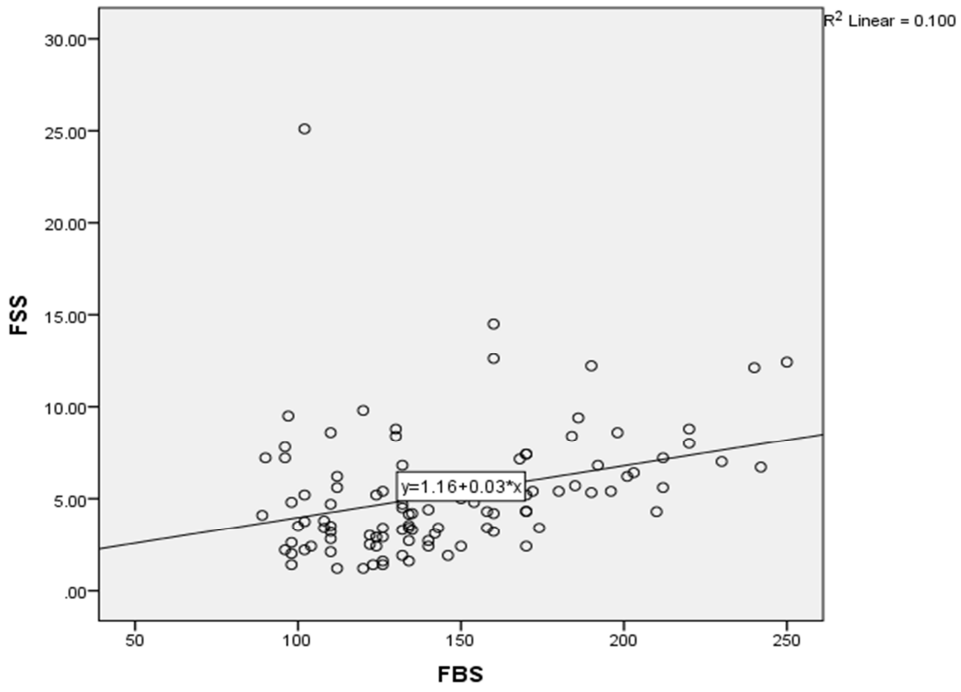

Table 5: Correlation of post prandial capillary sugar with post prandial salivary sugar

		PPSS
PPCS	Pearson Correlation	0.595
	p value	0.0001
	Inference	Positive correlation

We observed statistically significant positive correlation of post prandial capillary sugar with post prandial salivary sugar ($p<0.05$).

Figure 5: Scatter diagram showing Correlation of post prandial capillary sugar with post prandial salivary sugar

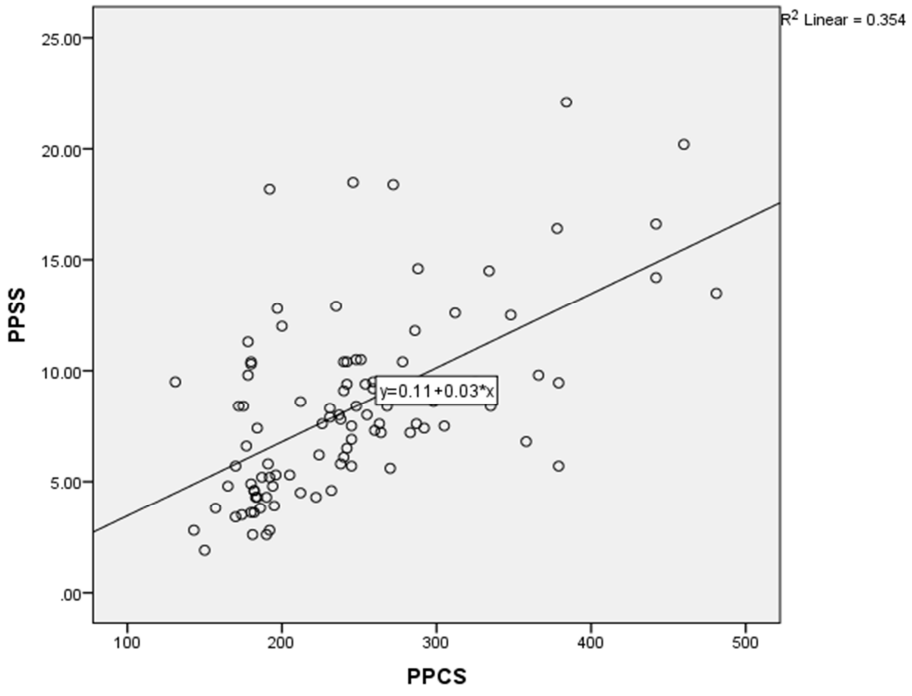

Table 6: Correlation of post prandial blood sugar with post prandial salivary sugar

		PPSS
PPBS	Pearson Correlation	0.59
	p value	0.0001
	Inference	Positive correlation

We observed statistically significant positive correlation of post prandial blood sugar with post prandial salivary sugar ($p<0.05$).

Figure 6: Scatter diagram showing Correlation of post prandial blood sugar with post prandial salivary sugar

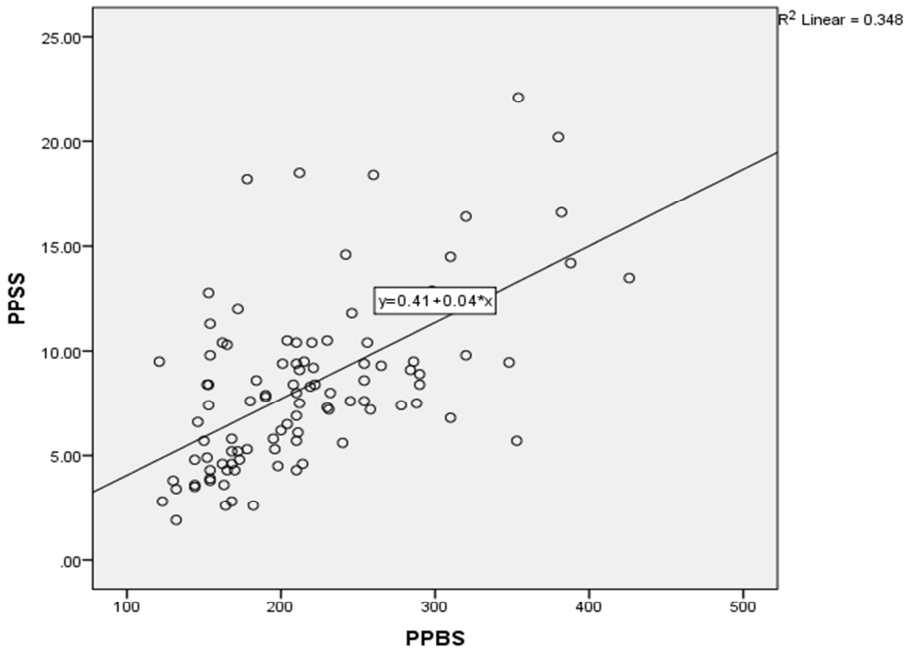

Table 7: Correlation of fasting salivary sugar with HBA1c

		HBA1c
FSS	Pearson Correlation	0.17
	p value	0.079
	Inference	Positive correlation

We observed statistically significant positive correlation of fasting salivary sugar with HBA1c ($p<0.05$).

Figure 7: Scatter diagram showing Correlation of fasting salivary sugar with HBA1c

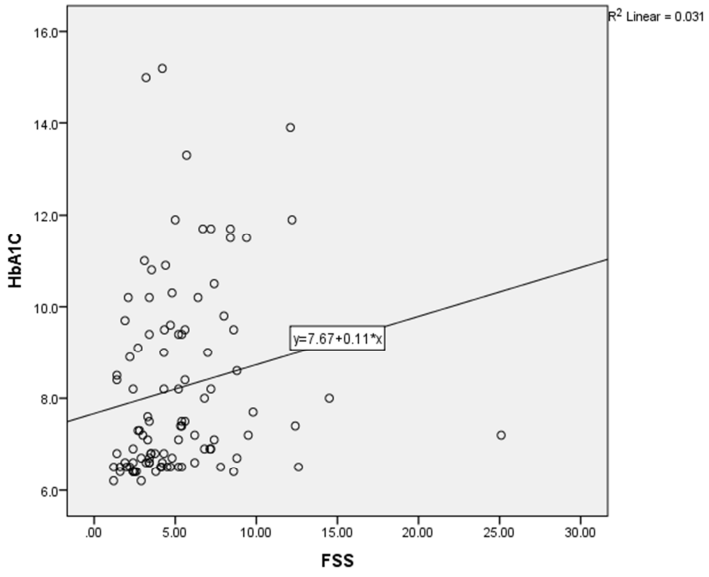

Table 8: Correlation of post prandial salivary sugar with HBA1c

		HBA1c
PPSS	Pearson Correlation	0.331
	p value	0.01
	Inference	Positive correlation

We observed statistically significant positive correlation of post prandial salivary sugar with HBA1c ($p<0.05$).

Figure 8: Scatter diagram showing Correlation of post prandial salivary sugar with HBA1c

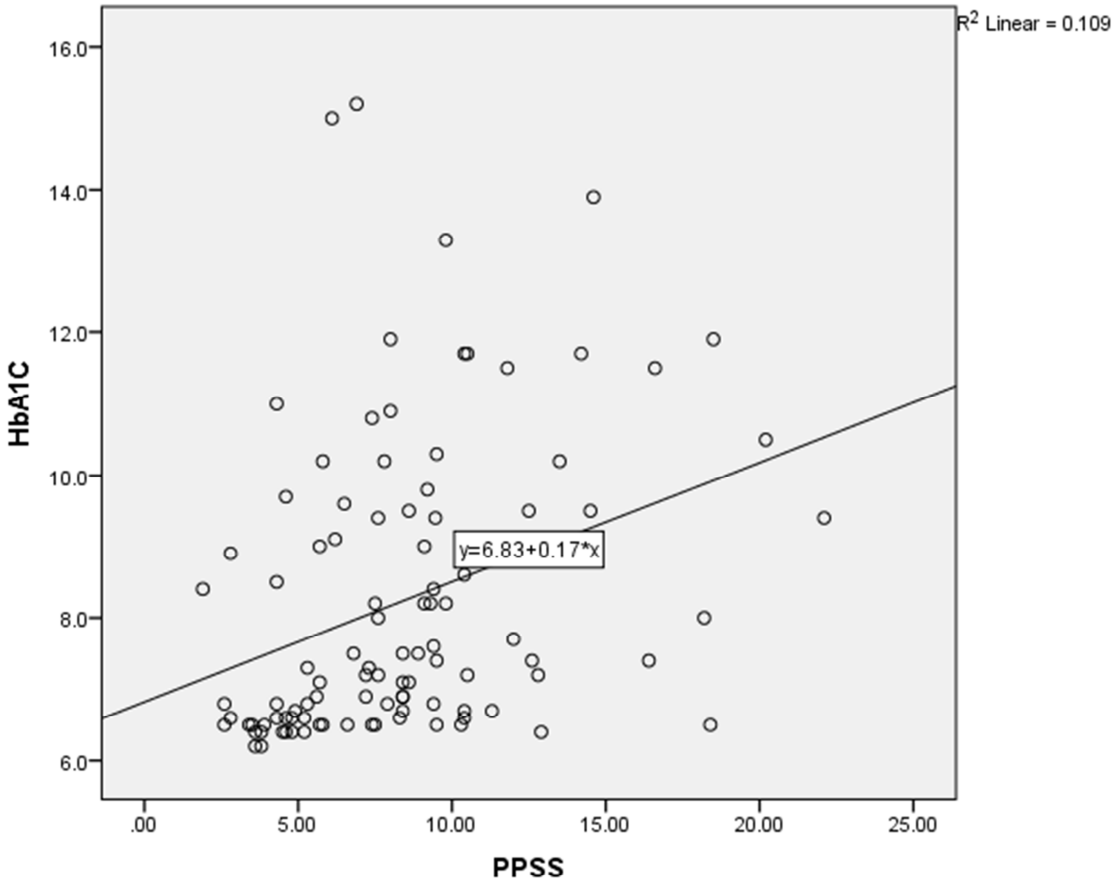

Table 9: Correlation of fasting salivary sugar with retinopathy

		N	Mean	SD	F	p	Inference
FSS	Mild NPDPR	30	6.00	4.52	1.36	0.22 (>0.05)	Not significant
	Moderate NPDPR	14	5.97	2.80			
	Severe NPDPR	1	12.10	--			
	PDR	1	3.40	--			
	HTN	1	2.20	--			
	Microaneurysms	1	5.70	--			
	BV attenuated	1	4.20	--			
	Normal	51	4.54	2.72			
	Total	100	5.22	3.45			

Mean values of fasting salivary sugar were given in the above table with respect to retinopathy. Mean value of FSS was higher in severe NPDPR i.e. 12.10±0 followed by 6.00±0 in mild NPDPR, 5.97±2.80 in moderate NPDPR. We compared the mean FSS values in different retinopathy conditions and the difference was found to be statistically non-significant ($p>0.05$). We observed that there was clinically elevated value of fasting salivary sugar in severe NPDPR though it does not showed statistical significance.

Figure 9: Correlation of fasting salivary sugar with retinopathy

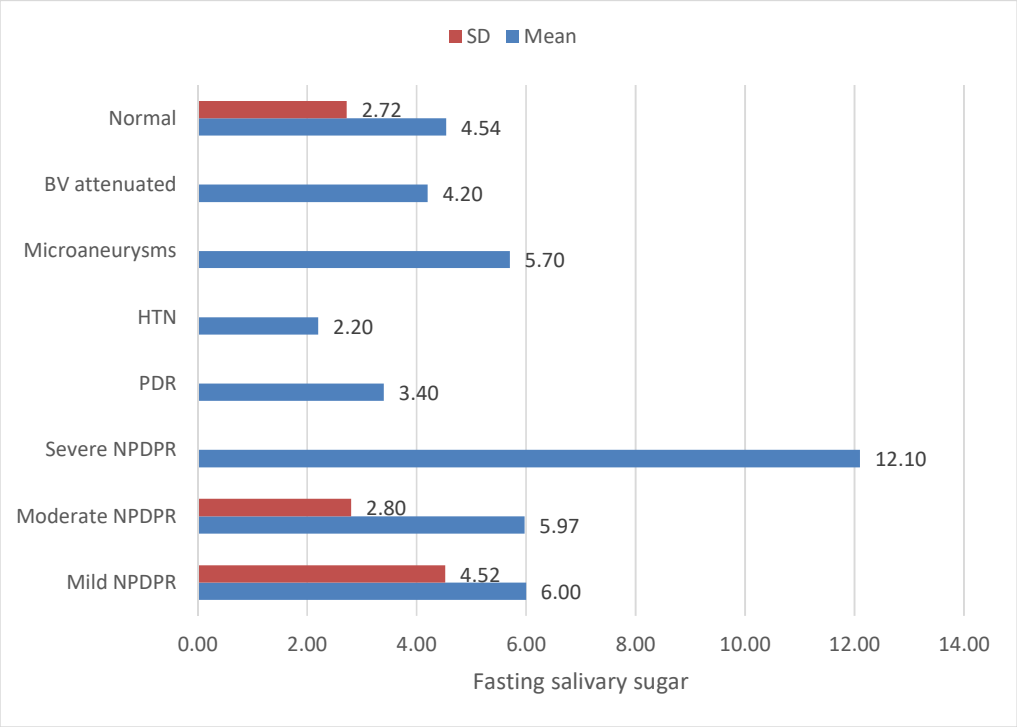

Table 10: Correlation of Postprandial salivary sugar with Retinopathy

		N	Mean	SD	F	p	Inference
PPSS	Mild NPDPR	30	9.23	3.97	2.3	0.03 (<0.05)	Significant
	Moderate NPDPR	14	10.68	5.00			
	Severe NPDPR	1	14.60	--			
	PDR	1	5.80	--			
	HTN	1	2.80	--			
	Microaneurysms	1	9.80	--			
	BV attenuated	1	6.90	--			
	Normal	51	7.20	3.53			
	Total	100	8.34	4.08			

Mean values of post prandial salivary sugar were given in the above table with respect to retinopathy. Mean value of PPSS was higher in severe NPDPR i.e. 14.60±0 followed by 10.68±5.0 in moderate NPDPR, 9.23±3.97 in mild NPDPR. We compared the mean PPSS values in different retinopathy conditions and the it was determined that the difference was statistically significant ($p<0.05$).

Figure 10: Correlation of Post prandial salivary sugar with Retinopathy

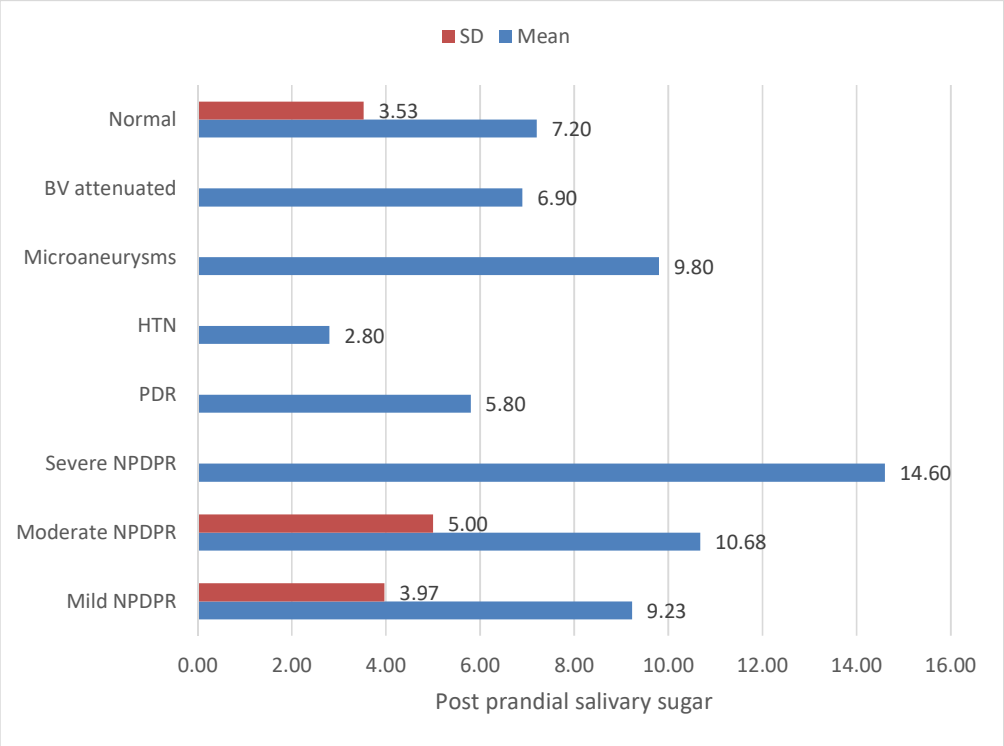

Table 11: Correlation of HBA1c with Retinopathy

		N	Mean	SD	F	p	Inference
HBA1c	Mild NPDPR	30	8.83	1.13	48.5	0.0001 (<0.05)	Highly Significant
	Moderate NPDPR	14	10.89	1.89			
	Severe NPDPR	1	13.90	--			
	PDR	1	10.20	--			
	HTN	1	8.90	--			
	Microaneurysms	1	13.30	--			
	BV attenuated	1	15.20	--			
	Normal	51	6.74	0.36			
	Total	100	8.22	2.07			

Mean values of HBA1c were given in the above table with respect to retinopathy. Mean value of HBA1c was higher in severe NPDPR i.e. 13.90±0 followed by 10.89± 1.89 in moderate NPDPR, 8.83±1.13 in mild NPDPR. We compared the mean HBA1c values in different retinopathy conditions and the difference was found to be statistically significant ($p<0.05$).

Figure 11: Correlation of HBA1c with Retinopathy

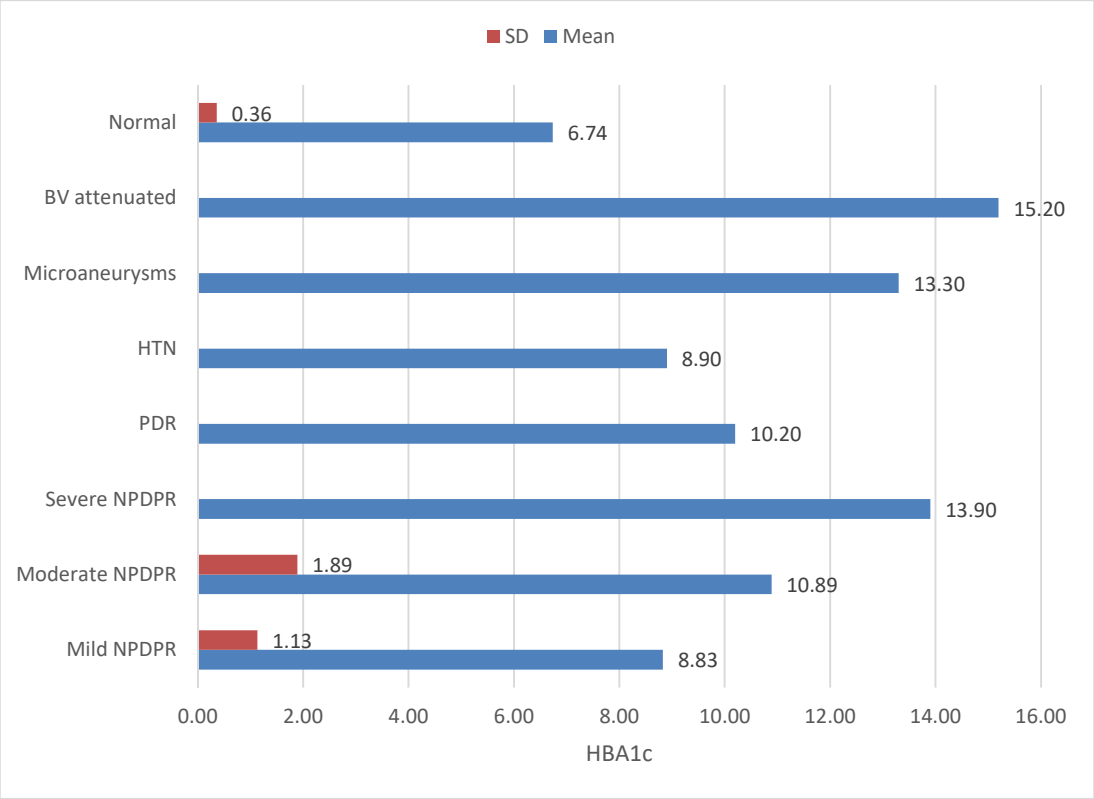

Table 12: Correlation of fasting and post prandial salivary sugar with all parameters

		FBS	**HbA1C**
FSS	Pearson Correlation	.317**	0.177
	p value	0.001	0.079
	Inference	Positive correlation	Positive correlation
		PPBS	**HbA1C**
PPSS	Pearson Correlation	.590**	.331**
	p value	0.0001	0.001
	Inference	Positive correlation	Positive correlation

We observed statistically significant positive correlation of fasting salivary sugar with fasting blood sugar ($p<0.05$) and there was weak positive correlation of fasting salivary sugar with HBA1c in our study ($p>0.05$).

A statistically significant positive connection was found in post prandial salivary sugar with post prandial blood sugar ($p<0.05$) and also with HBA1c in our study ($p<0.05$).

Discussion

Type 1 diabetes (IDDM) and type 2 diabetes (NIDDM) are the most common forms of the disease. Gestational diabetes, secondary diabetes, and young people's maturity-onset diabetes are the other forms of the disease. If routine monitoring is not carried out, chronic hyperglycemia can result in metabolic dysregulation and organ failure, particularly in the eyes, kidneys, nerves, heart, and blood vessels. However, because it involves the use of sharps and the assistance of a qualified technician, blood collection is a more expensive and invasive procedure.[40]

Therefore, developing a non-invasive method to check glycaemic control becomes necessary. Saliva is a fantastic adjuvant and plays a significant part in maintaining the oral cavity's homeostasis since it balances the environment there, making it a useful marker for the early diagnosis of many disorders. Salivary glucose seems to be the salivary parameter most closely associated with the oral environment in diabetic patients. Since glucose is a tiny molecule that diffuses rapidly across semipermeable membranes, it raises salivary glucose levels, which in turn causes a loss of homeostasis and increases vulnerability to oral illnesses. Saliva normally contains 0.5–1.00 mg/100 ml of glucose, which has little to no impact on dental health or ensure the growth of microorganisms. [40]

The use of saliva as a diagnostic fluid has grown over time, particularly in the field of clinical endocrinology, where it is easy and precise to assess the majority of unconjugated steroids, hormones, and antibodies. Due to its small size, glucose may easily diffuse across semi-permeable membranes, which is how it is found in saliva.

The altered salivary gland basement membrane that causes glucose to escape into saliva is the cause of the elevated glucose content in people with diabetes. [40]

Sociodemographic characteristics of the study population

We included confirmed cases of type II diabetes in our study. Our of 100 cases, majority were above 60 years age group i.e. 47%, followed by 32% in 51-60 yrs age group, 13% in 41-50 years age and 8% in 31-40 years age . Mean age of the study population was 60.6±13.01 years. 62% of the cases were males and 38% were females.

Cui Y et al[36] in their study reported that, " there were 14 males and 26 females with an average age of (50.1 ± 4.8) years in the patient group and 14 males and 26 females with an average age of (49.7 ± 3.7) years in the control group. No statistically significant differences were observed due to gender (t = 0.641, p = 0.289) or age (t = 0.181, p = 0.510) between the two groups."[36]

Dharmakeerthi et al[37] reported that**, "**a total of 120 DM patients (mean 51.5±7.36 years) with the age range of 25 — 60 years were participated in their study. 42.5% were from 46-55 years age group, 33.3% from 56-60 years, 24.2% from 20-45 years age group. 79.2% were females and 20.8% were males. Mean age of healthy individuals was 40.29±11.42 years with the age range of 23 — 60 years." [37]

Golamari UMR et al[39] in their study reported that, " out of the 200 study subjects, the mean age of the study population was 55.24 with the range of 27 to 85 years. The proportion of male and female subjects in our study were 105 (52.50%) and 95 (47.50%) respectively. "[39]

Afreen Nadaf et al[40] in 2017 conducted the study, "with the objective to assess the correlation of fasting blood glucose level (FBG) and fasting salivary glucose level (FSG) in diabetic and non-diabetic patients. An experimental study was conducted in 60 patients who fulfilled the selection criteria. Patients were categorized into 2 groups

-30 patients with diabetes mellitus (Group A) and 30 healthy non-diabetic patients (Group B). The fasting blood and unstimulated saliva samples were collected from the patients." [40]

Kumar K. et al[41] in 2017 conducted the study, "with the objective to study the correlation between salivary and blood glucose levels. Age matched 50 diabetic and 50 healthy non-diabetic individuals were included in the study. Structured questionnaire was used to know the educational status and knowledge about diabetes mellitus. The mean and standard deviation of age was 58.18 (10.13) years in diabetics and 54.08 (14.53) years in healthy subjects. There were 32 males and 18 females among diabetics and 26 males and 24 females among healthy subjects." [41]

Correlation of salivary and blood sugar

We observed statistically significant positive correlation of fasting capillary sugar with fasting salivary sugar($p<0.05$). We observed statistically significant positive correlation of fasting blood sugar with fasting salivary sugar ($p<0.05$). We observed statistically significant positive correlation of post prandial capillary sugar with post prandial salivary sugar ($p<0.05$). We observed statistically significant positive correlation of post prandial blood sugar with post prandial salivary sugar ($p<0.05$).

Cui Y et al[36] in their study reported that, "the population correlation that the UPS (unstimulated parotid saliva) had the highest glucose level and was most correlated with the blood glucose level. Besides, it can be better used to diagnose DM. Therefore, the UPS was used to study the individual correlation between blood glucose and salivary glucose. The average correlation coefficient between pre-prandial salivary glucose and blood glucose in DM patients was 0.88, and the average correlation coefficient between postprandial salivary glucose and blood glucose was

0.813, while the average correlation coefficient between pre-prandial salivary glucose and blood glucose in the control group was 0.78. The average correlation coefficient between postprandial salivary glucose and blood glucose was 0.7325. The correlation coefficients before and after breakfast for various individuals within a week varied significantly, the overall consistency was high. In general, the correlation coefficients before breakfast were higher than those after breakfast. " [36]

In comparison, our study had significant correlation in Fasting Salivary Sugar with fasting blood sugar and post prandial salivary sugar with post prandial blood sugar.

Dharmakeerthi et al[37] reported that, **"t**he moderate correlation coefficient was shown between blood glucose level and salivary glucose in l0x method ($r = 0.359$, $p < 0.001$). Salivary glucose level was significantly higher in DM patients than healthy individuals. Fasting blood glucose level was significantly correlated with salivary glucose levels among DM patients ($r = 0.201$, $p = 0.027$). Our study had significant correlation of FBS with FSS and PPBS with PPSS." [37]

Golamari UMR et al[39] in their study reported that, **"**the mean FBS of the study population was 159.98 with values ranging from 64 to 480 mg/dL. They found that there was statistically significant (r Value: 0.894, P-value). They also observed that there was statistically significant (r-value 0.751 and P-value < 0.001) strong positive correlation seen between FBS and salivary glucose in case group" [39]. In comparison , our study has only cases , controls were not included and the results obtained showed positive correlation of FSS with FBS and PPSS with PPBS .

Afreen Nadaf et al[40] reported that, **"**statistically significant difference (p=0.0001*) was found between the fasting salivary glucose (FSG) level between the 2 groups.

Correlation between FBG and FSG for Group A and Group B showed a very high significant difference (p= 0.001*)."[40]

In comparison , Our study also had similar results in correlation of FBS with FSS.

Kumar K. et al[41] in their study reported, "positive correlation between salivary and blood glucose level in diabetic (r-0.811, p-0.0001) and also in normal healthy individuals (r-0.51, p-0.0001). This shows that salivary glucose is capable of estimating 81% of blood glucose in diabetics." [41]

Gupta S. et al[42] in 2017 In the present study, "statistically significant correlation was found between salivary glucose level (SGL) and blood glucose level in patients with diabetes and controls as well." [42]

Akasapu A. et al[43] in 2017 stated**, "**200 subjects (100 subjects in each group) with the correlation coefficient between serum glucose and salivary glucose was calculated and the 'r' value was found to be 0.7686, which was highly significant (P value 0.01). These findings suggest that saliva can be used as a diagnostic tool in assessment of blood glucose concentration." [43]

"Consistent with our study, a significant correlation was found between salivary and blood glucose concentrations" by Amer S et al in Karachi.[55]

This result is consistent with earlier research conducted by Jurysta C et al[56], Hedge A et al[57] and Panda A et al[58]

These findings suggest that the amount of glucose in serum may influence the amount of glucose in saliva. Conversely, a few research have refuted the association found in blood and salivary glucose. However, a number of studies that are comparable to ours have demonstrated a strong association between PPBS and PPSS and FBS and FSS.

Therefore, it has been proposed that saliva may be used to measure a diabetic's blood glucose level. The examination of salivary glucose levels is an attempt to establish a painless and non-invasive way for diabetes patients to regularly monitor their blood glucose levels. Given the strong link found between salivary and blood glucose, more investigation is needed to confirm this as a trustworthy diagnostic method going forward.

In the present study, a significant correlation between FBG and FSG level was identified among DM patients. Our result is in good agreement with those reported by **Gupta et al**[58] and **Srikala et al.**[59]

Mishra et al[60] found, "a positive and statistically significant correlation between salivary and blood glucose in DM patients. Therefore, salivary glucose can be used to predict blood glucose level in DM patients."[60] **Karjalainen et al**[61] demonstrated that, "after good blood glucose control in DM patients, both salivary glucose and blood glucose are reduced to varying degrees, which suggests that salivary glucose and blood glucose have a certain correlation."[61]

"On the surface, saliva collection appears to be a simple, non-invasive technique; however, different collection methods have limits that are not always obvious. A range of organic and inorganic compounds are known to be secreted by the parotid gland. The saliva component is extremely viscous and simple to digest. However, UPS flow rates are relatively modest, and its collection takes some time. Because the submandibular and sublingual glands are so close to one another, they are commonly lumped together. As a result, it is difficult to reliably isolate saliva from these glands. As a result, saliva was collected from both glands at the same time in the current investigation."[46]

Since DM does not exhibit many symptoms in its early stages, the majority of people do not receive a diagnosis. The invasive blood sample collection process carries a high risk of consequences, including bleeding, hematoma, fainting, dizziness, and arterial punctures. To prevent these consequences, a non-invasive, accurate, patient-friendly technique is required.[37]

Numerous research investigations have demonstrated a noteworthy association between salivary and blood glucose levels, which can be useful for both diagnosis and glucose level monitoring. As a result, measuring salivary glucose levels offers a non-invasive solution to the issues associated with invasive methods like drawing blood to assess serum glucose levels. Human saliva contains a variety of substances that can be used for quick tests, including water, electrolytes, proteins, enzymes, immunoglobulins, and biomarkers. Consequently, it is proposed that the assessment of these components in saliva is crucial for next research aimed at determining disease diagnosis, as saliva is an ultrafiltrate of blood and blood biochemical changes have a direct impact on saliva. Saliva collection techniques are also simple and non-invasive. [37]

Consistent with the above studies our study also showed positive correlation between fasting capillary sugars, fasting blood sugar with fasting salivary sugar. There is positive correlation between post prandial capillary sugar , postprandial blood sugar with post prandial salivary sugar.

Our study correlated capillary sugar , venous sugar levels with salivary sugars and we have correlated salivary sugar with Hba1c levels also. As we found positive correlation between blood sugars with salivary sugars , we also correlated complications of diabetes i.e retinopathy with salivary sugar levels. We found

significant correlation between post prandial salivary sugar with retinopathy changes , but insignificant correlation between fasting salivary sugars and retinopathy changes.

We found positive correlation of fasting salivary sugars and post prandial salivary sugars with Hba1c .

Hence we consider our study is superior to many studies conducted as we correlated salivary sugars with many parameters like Hba1c and retinopathy changes as well.

So this study forms a basis for further projects to undertake in future in screening and monitoring of patients with diabetes mellitus.

Summary and conclusion

Summary

The present cross sectional Descriptive observational study was carried out at Department of General Medicine, KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi involving total 100 known cases of type 2 diabetes coming to IPD. The objective of our study was to correlate salivary glucose level with blood glucose level in diabetes mellitus patients at our tertiary care Centre.

The results of our study are summarized as follows:

- We included confirmed cases of type II diabetes in our study. Our of 100 cases, majority were from above 60 years age group i.e. 47% followed by 32% from 51-60 years age group i.e. followed by 13% from 41-50 years and 8% from 31-40 years. Mean age of the study population was 60.6±13.01 years. 62% of the cases were males and 38% were females. We observed statistically significant positive correlation of fasting capillary sugar with fasting salivary sugar($p<0.05$).
- Statistically significant positive correlation established that of fasting blood sugar with fasting salivary sugar ($p<0.05$).
- Statistically significant positive correlation established that of post prandial capillary sugar with post prandial salivary sugar ($p<0.05$).
- Statistically significant positive correlation established that of post prandial blood sugar with post prandial salivary sugar ($p<0.05$).
- Statistically significant positive correlation established that of fasting salivary sugar with HBA1c ($p<0.05$).
- Statistically significant positive correlation established that correlation of post prandial salivary sugar with HBA1c ($p<0.05$).

- Mean values of fasting salivary sugar were given in the table no.9 with respect to retinopathy. Mean value of FSS was higher in severe NPDPR i.e. 12.10±0 followed by 6.00±0 in mild NPDPR, 5.97±2.80 in moderate NPDPR. We compared the mean FSS values in different retinopathy conditions and the difference was found to be statistically non-significant ($p>0.05$). We found that there was clinically elevated value of fasting salivary sugar in severe NPDPR though it does not showed statistical significance.
- Mean values of post prandial salivary sugar were given in the table no.10 with respect to retinopathy. Mean value of PPSS was higher in severe NPDPR i.e. 14.60±0 followed by 10.68±5.0 in moderate NPDPR, 9.23±3.97 in mild NPDPR. We found the mean PPSS values in different retinopathy conditions and the difference was found to be statistically significant ($p<0.05$).
- Mean values of HBA1c were given in the above table no 11 with respect to retinopathy. Mean value of HBA1c was higher in severe NPDPR i.e. 13.90±0 followed by 10.89± 1.89 in moderate NPDPR, 8.83±1.13 in mild NPDPR. We compared the mean HBA1c values in different retinopathy conditions and the difference was found to be statistically significant ($p<0.05$).
- Statistically significant positive correlation established that of fasting salivary sugar with fasting blood sugar ($p<0.05$) and there was weak positive correlation of fasting salivary sugar with HBA1c in our study ($p>0.05$).
- Statistically significant positive correlation established that of post prandial salivary sugar with post prandial blood sugar ($p<0.05$) and also with HBA1c in our study ($p<0.05$).

Conclusion

- We got statistically significant positive correlation of fasting capillary sugar with fasting salivary sugar($p<0.05$). We observed statistically significant positive correlation of fasting blood sugar with fasting salivary sugar ($p<0.05$). We observed statistically significant positive correlation of post prandial capillary sugar with post prandial salivary sugar ($p<0.05$). We observed statistically significant positive correlation of post prandial blood sugar with post prandial salivary sugar ($p<0.05$).
- Based on the present study, we conclude that saliva can be used as a noninvasive test for glucose estimation, and it can be used as a screening test in diagnosing DM patients.
- Further studies with larger sample size may be useful for further correlation.

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CONSENT STATEMENT

I am making a voluntary decision to participate in the study "CORRELATION OF SALIVARY GLUCOSE LEVEL WITH BLOOD GLUCOSE LEVEL IN DIABETES MELLITUS" My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

CASE PROFORMA

PROFORMA FOR DATA COLLECTION

Name:_____

Age: _____ Sex:_____

Address:_____Phone

No._____

Occupation:_____

Reg. No. :_____

Chief Complaint:-

1)

2)

Presenting Complaints:

1. History:

2. Past History:

3. Family History:

4. Present medications:

5. Personal History:

Diet/ Appetite: Bowel/ Bladder habits:

Drug allergy:

6. Obstetric History (if significant):

7. General Physical Examination:

Consciousnes

Built

Nutrition

Pallor / Icterus / Cyanosis / Skin rash

Fundus examination

XANTHOMA

XANTHELESMA

ARCUS SENILIS

Pulse rate: Blood pressure:

Respiratory rate: Temperature:

Weight: Height:

Peripheral Pulses:

Flaps:

8. Systemic Examination:

ABDOMEN:

RESPIRATORY SYSTEM:

CARDIOVASCULAR SYSTEM:

CENTRAL NERVOUS SYSTEM:

9. CLINICAL DIAGNOSIS:

10. INVESTIGATIONS:

FBS- Venous

FBS - Capillary

Fasting Salivary glucose

PPBS- Venous

PPBS - Capillary

Post prandial salivary glucose

SR NO	IP/OP NO.	AGE	GENDER	FCS	FBS	FSS	PPCS	PPBS	PPSS	HbA1C	FUNDOSCOPY
1	10037088	51	F	210	190	12.2	246	212	18.5	11.9	B/L MOD NPDR
2	10035996	80	M	100	96	7.2	240	220	10.4	11.7	B/L MOD NPDR
3	10038303	58	M	142	120	9.8	200	172	12	7.7	NORMAL
4	10039171	45	M	275	240	12.1	288	242	14.6	13.9	B/L SEVERE NPDR
5	10038511	75	M	109	97	9.5	197	153	12.8	7.2	NORMAL
6	10039040	55	M	135	110	8.6	235	298	12.9	6.4	NORMAL
7	10038508	51	M	99	96	7.8	131	121	9.5	6.5	NORMAL
8	10039568	68	F	244	220	8	259	221	9.2	9.8	RE MILD NPDR
9	10038982	77	F	142	130	8.8	242	210	10.4	6.7	NORMAL
10	10039775	78	M	108	90	7.2	178	154	9.8	8.2	LE MILD NPDR
11	10039508	85	M	177	160	14.5	192	178	18.2	8.0	B/L MILD NPDR
12	10039720	56	F	158	140	5.2	240	212	9.1	8.2	RE MILD NPDR
13	10036235	70	F	235	180	5.4	335	290	8.4	7.5	B/L MOD NPDR
14	10037812	35	M	165	150	2.4	212	198	4.5	6.4	NORMAL
15	10038603	45	F	247	185	5.7	366	320	9.8	13.3	BE MICRO ANEURYSMS
16	10038196	80	M	188	140	2.4	283	258	7.2	6.9	NORMAL
17	10037205	65	M	120	96	2.2	143	123	2.8	8.9	B/L GRADE 1 HTN RETIONOPATHY
18	10038135	73	M	134	126	1.4	150	132	1.9	8.4	B/L MILD NPDR
19	10042051	55	M	182	158	3.4	238	195	5.8	10.2	B/L PDR
20	10042081	52	F	185	160	4.2	245	210	6.9	15.2	B/L BV ATTENUATED
21	10043794	78	M	193	150	5	255	232	8	11.9	B/L MOD NPDR
22	10044559	65	F	140	122	3	226	180	7.6	7.2	NORMAL
23	10042929	70	F	132	120	1.2	157	130	3.8	6.2	NORMAL
24	10042608	73	M	150	134	3.4	321	290	8.9	7.5	B/L MILD NPDR
25	10044392	71	M	130	112	1.2	170	132	3.4	6.5	NORMAL
26	10044287	55	M	164	140	4.4	237	210	8	10.9	B/L MILD NPDR
27	10043807	65	M	139	126	2.9	180	144	3.6	6.2	NORMAL
28	10044381	52	F	168	154	4.8	259	215	9.5	10.3	B/L MOD NPDR

29	10043303	53	M	190	160	3.2	240	211	6.1	15.0	B/L MOD NPDR
30	10040708	55	F	112	102	5.2	180	165	10.3	6.5	NORMAL
31	10044306	70	M	148	108	3.8	192	172	5.2	6.4	NORMAL
32	10044544	62	F	156	130	8.4	251	230	10.5	11.7	B/L MILD NPDR
33	10043661	60	M	221	203	6.4	481	426	13.5	10.2	B/L MILD NPDR
34	10044225	43	F	159	135	4.2	231	219	8.3	6.6	NORMAL
35	10044695	61	M	196	170	2.4	291	265	9.3	8.2	B/L MILD NPDR
36	10043274	48	M	160	146	1.9	232	214	4.6	9.7	B/L MOD NPDR
37	10042923	56	M	154	143	3.4	184	170	4.3	6.6	NORMAL
38	10043848	72	M	199	168	7.14	270	240	5.6	6.9	B/L NPDR
39	10040865	43	F	150	134	4.16	190	182	2.6	6.5	NORMAL
40	10043809	31	F	130	122	2.5	182	162	4.6	6.4	NORMAL
41	10043604	72	M	195	170	4.33	334	310	14.5	9.5	B/L MILD NPDR
42	10044247	64	F	116	102	3.75	196	178	5.3	6.8	NORMAL
43	10044318	55	F	151	132	1.9	192	168	2.8	6.6	NORMAL
44	10044942	52	F	142	134	1.6	186	154	3.8	6.4	NORMAL
45	10044877	82	M	140	124	2.9	180	152	4.9	6.7	NORMAL
46	10044475	61	M	261	230	7	310	284	9.1	9.0	B/L MILD NPDR
47	10044670	61	M	210	190	5.33	325	286	9.5	7.4	B/L MOD NPDR
48	10044816	64	F	168	134	3.54	292	278	7.4	10.8	B/L MOD NPDR
49	10043703	55	M	225	196	5.4	379	348	9.46	9.4	B/L MILD NPDR
50	10045102	53	F	164	135	3.3	245	210	5.7	7.1	B/L MILD NPDR
51	10043387	80	M	128	124	2.4	182	163	3.6	6.4	NORMAL
52	10043247	60	M	111	102	2.2	195	154	3.9	6.5	NORMAL
53	10045141	57	M	158	132	4.7	242	204	6.5	9.6	B/L MILD NPDR
54	10044534	54	M	125	110	3.2	187	168	5.2	6.6	NORMAL
55	10045014	75	M	128	98	2.6	194	173	4.8	6.4	NORMAL
56	10039440	85	M	138	110	3.5	190	154	4.3	6.8	NORMAL
57	10041316	78	M	168	134	2.7	205	196	5.3	7.3	NORMAL
58	10044076	43	M	145	126	1.6	305	288	7.5	6.5	NORMAL
59	10044117	67	M	177	158	4.3	231	190	7.9	6.8	NORMAL

60	10038647	90	M	110	89	4.1	170	150	5.7	6.5	NORMAL
61	10044127	70	M	146	124	5.2	384	354	22.1	9.4	B/L MILD NPDR
62	10044937	60	M	264	242	6.7	442	388	14.2	11.7	B/L MOD NPDR
63	10044878	59	M	169	140	2.7	224	200	6.2	9.1	B/L MILD NPDR
64	10044898	68	F	255	210	4.3	379	353	5.7	9	B/L MILD NPDR
65	10044511	71	F	143	123	1.4	222	210	4.3	8.5	B/L MILD NPDR
66	10044082	62	M	148	110	2.8	260	230	7.3	7.3	B/L MILD NPDR
67	10044629	65	M	125	104	2.4	165	144	4.8	6.6	NORMAL
68	10044872	67	F	236	186	9.4	286	246	11.8	11.5	B/L MOD NPDR
69	10045044	84	M	294	250	12.4	378	320	16.4	7.4	NORMAL
70	10044463	61	F	133	112	5.6	254	210	9.4	8.4	B/L MILD NPDR
71	10044773	68	M	210	198	8.6	348	286	12.5	9.5	B/L MILD NPDR
72	10044965	86	M	204	184	8.4	442	382	16.6	11.5	B/L MOD NPDR
73	10007693	65	F	130	110	2.1	238	190	7.8	10.2	B/L MILD NPDR
74	10007995	57	M	198	174	3.4	287	254	7.6	9.4	B/L MILD NPDR
75	10008093	39	F	199	170	4.3	245	212	7.5	8.2	B/L MILD NPDR
76	10008067	48	F	240	212	5.6	358	310	6.8	7.5	NORMAL
77	10008420	58	F	165	142	3.1	183	165	4.3	11	B/L MOD NPDR
78	10008054	41	F	109	98	2	174	144	3.5	6.5	NORMAL
79	10008112	68	F	138	126	3.4	182	168	4.6	6.6	NORMAL
80	10064884	60	M	183	170	5.2	248	208	8.4	7.1	NORMAL
81	10006953	61	M	242	212	7.2	268	222	8.4	6.9	NORMAL
82	10008147	48	M	228	201	6.2	264	231	7.2	7.2	NORMAL
83	10008398	51	M	200	172	5.4	312	284	12.6	7.4	NORMAL
84	10005316	55	M	190	160	12.6	272	260	18.4	6.5	NORMAL
85	1133274	35	F	144	132	6.8	175	152	8.4	6.9	NORMAL
86	1142826	50	F	119	100	3.5	242	201	9.4	6.8	NORMAL
87	1136098	50	M	149	132	3.3	284	254	9.4	7.6	NORMAL
88	1132808	35	F	127	112	6.2	180	162	10.4	6.6	NORMAL
89	1134209	65	F	144	126	5.4	177	146	6.6	6.5	NORMAL
90	1135454	50	M	120	108	3.4	172	153	8.4	6.7	NORMAL

91	1134736	56	F	110	98	1.4	181	164	2.6	6.8	NORMAL
92	1127381	40	F	153	132	4.5	184	153	7.4	6.5	NORMAL
93	1143864	56	M	117	102	25.1	248	204	10.5	7.2	B/L MILD NPDR
94	1133372	40	M	111	98	4.8	178	154	11.3	6.7	NORMAL
95	1132772	55	M	130	110	4.7	191	168	5.8	6.5	NORMAL
96	1135856	65	M	182	170	7.4	212	184	8.6	7.1	NORMAL
97	1134811	58	F	243	220	8.8	278	256	10.4	8.6	B/L MILD NPDR
98	1134032	35	F	181	170	7.4	460	380	20.2	10.5	B/L MOD NPDR
99	1133446	54	M	159	134	5.6	298	254	8.6	9.5	B/L MILD NPDR
100	6565438	45	M	210	192	6.8	263	245	7.6	8	B/L MILD NPDR